REMARKS

Applicants respectfully request entry of the foregoing and continued examination of the subject matter identified in caption, as amended, pursuant to and consistent with 37 C.F.R. § 1.111, and in light of the remarks which follow.

As stated in the Office Action Summary, Claims 1-4, and 7-8 are pending.

Applicants note with appreciation that, as indicated in the Office Action Summary, the rejections made under 35 U.S.C. § 112, first paragraph, have been withdrawn.

Rejections under 35 U.S.C. § 102

Claims 1-4 stand rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Keller et al. ("Keller") (WO 9834595). Applicants traverse.

Applicants submit that Keller fails to teach each and every element of the claimed invention. As the Office knows, to anticipate a claimed invention under §102, a reference must teach each and every element of the claimed invention. *See Lindeman Machinenfabrik GmbH v. American Hoist and Derrick Company*, 221 USPQ 481, 485 (Fed. Cir. 1984).

Keller discloses an inhalable medicinal aerosol formulation comprising an effective amount of a pharmaceutically active compound and a pressure-liquified homogeneous propellant mixture, comprising carbon dioxide and hydrofuoroalkane, where the pharmaceutically active compound is either a beta-mimetic or a corticoid.

As noted by the Office on page 4 of the Office Action Summary, Keller does not disclose the employment of the inhalable medicinal aerosol composition comprising the combination as is presently claimed in a method for the treatment of asthma bronchiale for simultaneous, sequential or separate administration. Furthermore, Keller does not disclose a process for the preparation of the inhalable medicinal aerosol composition therein.

As noted above, anticipation requires that every element must be disclosed or recited by the reference. Keller does not anticipate the subject matter of the present invention, as it fails to teach the employment of the inhalable medicinal aerosol composition, and fails to disclose a process for the preparation of the inhalable

medicinal aerosol composition, as claimed in the present invention. As such, Keller fails to meet the requirements for anticipation as set forth under 35 U.S.C. § 102(b).

In light of the above, Applicants request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 7-8 stand rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over Keller, in view of Doi, Koji (WO 9831343)("Doi"), Bjermer ("Bjermer"), and van der Molen ("van der Molen"). Applicants note that the Office Action refers to the cited reference, "Bjerkec," however, Applicants believe that this is a typographical error, and the Office meant the reference, "Bjermer."

Keller purportedly discloses an inhalable medicinal aerosol composition or formulation comprising an effective amount of a beta-mimetics which is salbutamol, reproterol, almeterol, or formoterol, and an effective amount of a corticoids which is loteprednol. Doi purportedly discloses that loteprednol etabonate is known to be useful in a pharmaceutical composition and a method of treating inflammatory conditions or allergy since loteprednol etabonate has excellent anti-inflammatory and anti-allergic activities. Bjermer purportedly discloses that long-acting agonists are bronchospasmolytics and are used as inhalations in asthma treatment. Furthermore, Bjermer purportedly discloses that these agonists should always be given in combination with corticosteroids. Van der Molen purportedly discloses that the symptoms of asthma patients are improved on inhalation of the long-acting β_2 agonist, formmoterol in addition to inhaled corticosteroids. Van der Molen does not specify corticosteroids used. Thus, the Office maintains that it would have been obvious to employ loteprednol etabonate in combination with reproterol, salmeterol, or formoterol in a method for the treatment of allergies and/or airway disorders such as asthma brochiale for simultaneous, sequential or separate administration. Applicants traverse.

For a *prima facie* case of obviousness, the following three requirements must be met. First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or

incentive that would have motivated the skilled artisan to modify a reference or to combine the reference with another reference. Second, the proposed modification must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. Third, the prior art reference must teach or suggest all the limitations of the claims. The teachings or suggestions, as well as the expectation of success, must come from the prior art and not from applicant's disclosure. *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988); *Amgen, Inc. v. Chugai Pharm. Co.,* 927 F.2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991); and *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991).

The cited references as discussed below fail to recite all of the elements of the presently claimed invention and fail to provide an expectation of success or motivation to arrive at the claimed invention. The failings of the references, alone and in combination, are addressed in detail below.

Taken together, Keller, Doi, Bjerkec, and van der Molen fail to meet the requirements for a prima facie case of obviousness. The cited references do not disclose or suggest each and every element of the claimed invention. Furthermore, Keller, Doi, Bjerkec and van der Molen fail to suggest any motivation for one skilled in the art to modify or combine the teachings disclosed therein. From the disclosures in the cited references, a skilled artisan would not have a reasonable expectation of success to modify such disclosures therein.

The distinctions between the disclosures of Keller and the present invention, as discussed *supra*, are incorporated herein. In summary, Keller does not disclose the employment of the inhalable medicinal aerosol composition comprising the combination as is presently claimed in a method for the treatment of asthma bronchiale for simultaneous, sequential or separate administration and fails to disclose a process for the preparation of the inhalable medicinal aerosol composition therein.

Doi, Bjerkec, and van der Molen fail to satisfy the deficiencies of Keller. Doi is directed to the use of loteprednol etabonate for the treatment of inflammatory or allergic disease only. Asthma bronchiale or even related conditions are <u>not</u>

disclosed in Doi as being treated by loteprednol. Instead, classical steroids are disclosed for the treatment of asthma.

Bjerkec and van der Molen disclose the supplementation of inhalative therapy of asthma bronchiale with "classical" corticosteroids by long-time β_2-adrenoreceptor agonists. However, loteprednol is not a "classical" corticosterioid in the context of Bjermer and van der Molen, and thus does not apply to Bjermer and van der Molen.

Applicants again note the significant differences between "classical" steroids and loteprednol. Classic steroids cannot be extrapolated to soft steroids, such as loteprednol, as there are different mechanistic properties between these two groups of steroids. Further, loteprednol exhibits less side effects, improved therapeutic breadth and an overadditive therapeutic effect in combination with the disclosed ÿ2-adrenoreceptor agonists. However, none of the references disclose any of these advantages for loteprednol, whether used alone or in combination with a ÿ2-adrenoreceptor.

The Office asserts that it would be obvious to a person skilled in the art to combine the teachings of Keller with the teachings of the prior cited literature, Doi, Bjerkec, and van der Molen. However, the focus of the invention in Keller is quite different than that of the present invention. The focus of Keller is a pressure-liquified propellant mixture comprising fluorinated alkanes for the purpose of cosmetic and household spray. Keller fails to disclosure the certain pharmaceutical preparations for the treatment of respiratory or allergic diseases of the present invention. Thus, it would not have been obvious to combine the teachings of Keller with Doi, Bjerkec, and van der Molen.

In conclusion, Applicant submits that the cited references, Keller, Doi, Bjerkec and van der Molen, alone or in combination, fail to meet the requirements for a *prima facie* case of obviousness. The cited references fail to contain any motivation to modify said references, fail to disclose each and every one of the elements in the presently claimed invention, and further lack any reasonable expectation of success, should the references be so viewed. Therefore, Applicants request that the rejections under 35 U.S.C. § 103 be withdrawn.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

BUCHANAN INGERSOLL PC
(INCLUDING ATTORNEYS FROM BURNS, DOANE, SWECKER & MATHIS)

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By: Kim E. Choate
Kim E. Choate
Registration No. 57,102

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620